CALIFORNIA ENVIRONMENTAL PROTECTION AGENCY
DEPARTMENT OF PESTICIDE REGULATION
MEDICAL TOXICOLOGY BRANCH

# SUMMARY OF TOXICOLOGY DATA
# CARBOLIC ACID (PHENOL)

Chemical Code # 000107 , Tolerance # 50293
SB 950 # 555

Original date: 8/27/98

## I. DATA GAP STATUS

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| Chronic toxicity, rat: | Data gap, no study on file. |
| Chronic toxicity, dog: | Data gap, no study on file. |
| Oncogenicity, rat: | Data gap, inadequate study on file, possible adverse effect indicated (both chronic and oncogenic). |
| Oncogenicity, mouse: | Data gap, inadequate studies on file, possible adverse effect indicated (Dermal). |
| Reproduction, rat: | Data gap, no study on file. |
| Teratology, rat: | Data gap, inadequate study, no adverse effect indicated |
| Teratology, mice | Data gap, inadequate study, no adverse effect indicated |
| Gene mutation: | No data gap, possible adverse effects |
| Chromosome effects: | Data gap, inadequate study, possible adverse effect indicated |
| DNA damage: | Data gap, inadequate studies, no adverse effect indicated |
| Neurotoxicity: | Not required at this time. |

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Toxicology one-liners are attached.
All record numbers through 152764; volume 13 were examined.
** indicates an acceptable study.
**Bold face** indicates a possible adverse effect.
Phenol is grouped with sodium phenate, CC: 2164
File name: T980827
Prepared by J. Gee, August 27, 1998
**NOTE:** Brief comments (no worksheets) on publications relating to phenol are contained at the end under “Other” of this Toxicology Summary.

## II. TOXICOLOGY ONE-LINERS AND CONCLUSIONS

These pages contain summaries only. Individual worksheets may contain additional effects.

## GENERAL

011 152747 "Criteria for a recommended standard - occupational exposure to phenol." (Dept. of Environ. and Industrial Health, Michigan Univ., HEW Publication No. 76-196, July 1976) This document was prepared for NIOSH, Cincinnati, OH, for exposure to phenol. The document covers a number of aspects of exposure to phenol including acute toxicity, carcinogenicity and promotion, and work practices. The bibliography contains 349 citations, many of them quite dated. A number of these citations relate to human exposure, through accidents, mis-treatment, etc. Phenol is absorbed rapidly through the skin and excreted by several pathways. Also, some phenol is formed during normal metabolism. The primary routes of exposure in the workplace are through inhalation and/or the skin. (Gee, 8/20/98)

## CHRONIC TOXICITY, RAT

No study on file.

## CHRONIC TOXICITY, DOG

No study on file.

## ONCOGENICITY, RAT

**012 152749** Campbell, L. A., S. S. Olin, R. L. Schueler, D. J. Beach, A. C. Jacobs, W. D. Theriault and M. W. Glasser. "Bioassay of Phenol for Possible Carcinogenicity." (Hazleton Laboratories, VA, for National Cancer Institute & National Toxicology Program, NIH Publication No. 80-1759, August 1980.) Phenol (approximately 98.5%) was administered at concentrations of 0, 2500 or 5000 ppm in the drinking water to 50 F344 rats and 50 B6C3F1 mice/sex/group for 103 weeks. Water consumption and body weight were reduced for mice - NOEL <2500 ppm. Body weight (high dose) and water consumption (slight) were reduced (high and low dose groups) for rats - NOEL <2500 ppm. **Possible adverse effect**: a significant increase in the incidence of monocytic leukemia observed only for the low dose group suggests an association with the administration of phenol in the male rat. In addition, the incidence of kidney chronic inflammation was significantly increased at 5000 ppm in both sexes of the rat. UNACCEPTABLE (no stability in water or how often dosing water was prepared, no body weights, no water consumption data, no individual data for any parameter including histopathology). Not upgradeable as a chronic study (no hematology, clinical chemistry, urinalysis, or ophthalmology, two doses only with no NOEL). Doubtful as an oncogenicity study (no organ weights, no blood smears or hematology, other deficiencies as noted above) . (Kishiyama and Gee, 8/20/98)**.**

## ONCOGENICITY, MOUSE

See under -012 152749 above under rat oncogenicity. The possible adverse effect was identified in the rat but not the mouse. (Gee, 8/26/98)

**13 152754** Boutwell, R. K. and D. K. Bosch. "The Tumor-promoting Action of Phenol and Related Compounds for Mouse Skin." *Cancer Research*, 19: 413 - 429 (1959) Phenol (purified) was applied to the once-shaved skin on the back of mice from four sources: Arthur Sutter of Springfield, MO, Holtzman Rat Co., U. of Wisconsin and Jackson Laboratory. Both males and females were used in different assays. Experiments were performed with and without initiation with a single application of 75 ug DMBA. Papillomas greater than 1 mm were counted. Phenol was applied twice a week for varying lengths of time in acetone or in benzene at concentrations of 5%, 10% or 20%. In mice pretreated with DMBA, 10% phenol was much more effective at promoting papillomas than 5% phenol. At 36 weeks, the incidence in mice treated with phenol only was 25% for 10% phenol but only 1 mouse with 5% phenol had a papilloma. At 52 weeks, the incidence of carcinomas in mice initiated with DMBA and treated with 10% phenol was 47% with none in the DMBA only group. With the DMBA/croton oil control, the comparable incidence was 76%. In a comparison of the response of strains of mice to DMBA/phenol, Holtzman were more responsive than either $CAF_1$ or C3H mice with the maximum incidence of papillomas being 3.4, 1.4 and 0.7, respectively. The activity of phenol was compared with a number of related chemicals with various substitutions. The response of mice varied with the substitution and position. Results were presented that application of phenol alone at 2.5 mg (10% solution) twice weekly for a period of 24 weeks caused an incidence of papillomas in 95% of survivors. At 5 mg (20% solution), the incidence was 90% of survivors but the survival rate was lower due to toxicity of the phenol. At 1.25 mg (5%), the incidence was 56%. With an increase in the length of applications (e.g. 40 weeks), the incidence of carcinomas increased at 10 and 20% phenol without initiation. The conclusion was that with DMBA/10% phenol, papillomas occurred rapidly in large numbers with carcinomas appearing more slowly. Phenol alone was capable of causing tumors. **Possible adverse effect**. SUPPLEMENTAL study. No worksheet. (Gee, 8/27/98)

**13 152758** M. H. Salaman and O. M. Glendenning. "Tumor Promotion in Mouse Skin by Sclerosing Agents." *British Journal of Cancer*, 11: 434 - 444 (1957) "S" strain male mice were used to determine the promoting effect of phenol following initiation with DMBA. Two experiments were conducted. EXPT I: Four groups: 1) DMBA (0.2 ml of 0.15%) followed by 0.025 ml of 20% phenol in weekly applications for 24 weeks, alternating among 4 sites; 2) as for "1" without DMBA; 3) DMBA followed by 0.1 ml of 5% phenol alternating between anterior and posterior back skin for 32 weeks; 4) as in "3" without DMBA. Results of expt. I: 20% phenol caused local ulceration which healed over 4 weeks time but 5% caused only transient crusting. In group 1 at termination at 39 weeks, 11/13 mice had tumors with a total of 74 tumors, including 5 malignant tumors. In group 3, 4/14 had tumors with a total of 9 tumors with 2 malignant. With 20% phenol only, 7 tumors in 18 survivors arose with none malignant. In group 4, 5% phenol, no tumors occurred. EXPT II: Six groups of 20 male mice, "S" strain, were exposed to : 5, 6, and 7; DMBA followed by intradermal injection of proflavine, ethanolamine oleate and phenol (0.1 ml of 0.5% for 12 weeks followed by 1% for an additional 12 weeks); 8, 9, 10; no DMBA. Results of expt. II with phenol: group 7 - 5 tumors on 2/20 mice at week 23; group 10 (intradermal phenol) - no tumors. Conclusion: phenol was a "potent" promotor of tumors but a weak carcinogen in the presence of considerable dermal injury to all layers of the skin, as noted histologically. **Possible adverse effect.** SUPPLEMENTAL study. No worksheet. (Kishiyama, and Gee, 8/28/98)

013 152750 Van Duuren, B.L., T. Blazej, B.M. Goldschmidt, C. Katz, S. Melchionne, and A. Sivak. "Carcinogenesis Studies on Mouse Skin and Inhibition of Tumor Induction." *Journal of National Cancer Institute*, 46 (5): 1039 - 1044 (1971) Female ICR/Ha Swiss mice, 20/group, were exposed to benzo(a)pyrene, 5 ug, as the initiator and to a series of compounds to study the effects of simultaneous administration to the shaved skin three times per week over a period of 67 weeks. Phenol was one of the compounds tested at 3 mg in 0.1 ml of acetone. Tumors were recorded and those greater than 1 mm in diameter were recorded. Only those persisting for more

than 30 days were included in the total. With BaP alone, the incidence of the number of mice with papillomas and carcinomas was 8 and 1, respectively. When applied simultaneously with phenol, the incidence was 3 and 1 respectively. The authors concluded that phenol reduced the incidence of tumors under the experimental conditions. As controls, the simultaneous application of BaP and PMA (phorbol myristate acetate, 2.5 ug) resulted in an incidence of 20 animals with papillomas (total of 128 papillomas) and 13 animals with carcinomas. SUPPLEMENTAL study. No worksheet. (Kishiyama and Gee, 8/26/98)

013 152751 Van Duuren, B.L. and B.M. Goldschmidt. "Cocarcinogenic and Tumor-Producing Agents in Tobacco Carcinogenesis". *Journal of National Cancer Institute*, 56 (6): 1237 - 1242 (1976). Phenol at 3 mg and Benzo[a]pyrene (BaP) at 5 µg/0.1 ml acetone were applied three times/week (368 days) to the shaved areas of 50 female ICR/Ha Swiss mice and evaluated for cocarcinogenic activity. Both chemicals were contained in the same solution for simultaneous application. The incidence of skin tumors greater than 1 mm and persisting for 30 days were counted in the total. With BaP alone in acetone, the incidence of mice with papillomas/total papillomas (mice with squamous carcinomas) was 14/16 (10). The incidence was reduced when phenol was combined with Benzo[a]pyrene (BaP) compared to BaP alone with 7/9 (3). Phenol alone yielded 1/1 (0). Three of the simple phenols (phenol, resorcinol and hydroquinone) inhibited carcinogenesis and two (catcechol and pyrogallol) were considered active. SUPPLEMENTAL study. No worksheet. (Kishiyama and Gee, 8/26/98)

## REPRODUCTION, RAT

No study on file

## TERATOLOGY, RAT

010 152745: Jones-Price, C., T.A. Ledoux, J. R. Reel, P.W. Fisher, L. Langhoff-Paschke and M.C. Marr. "Teratological Evaluation of Phenol (CAS No. 108-95-2) in CD Rats." Research Triangle Institute, Study Code No.: Rt 80-2D. July 29, 1983. Phenol, 99.9% purity, was administered by gavage at concentrations of 0 (distilled water), 30, 60 or 120 mg/kg/day to 23 mated, CD rats/group during gestation days 6 through 15. Maternal NOEL = 120 mg/kg/day. [Doses at 125 mg/kg/day and higher caused mortality in preliminary studies]. High dose fetal body weight was reduced 7%; Developmental NOEL = 60 mg/kg/day (lower fetal body weight). UNACCEPTABLE, upgradeable. ( no individual data). (Kishiyama and Gee, 8/19/98)
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## TERATOLOGY, MOUSE

009 152727 Jones-Price, C., T.A. Ledoux, J. R. Reel, L. Langhoff-Paschke and M.C. Marr. "Teratological Evaluation of Phenol (CAS No. 108-95-2) in CD-1 Mice." ( Research Triangle Institute, Mi 80-2D, July 29, 1983). Phenol, 99.9% purity, was administered by oral gavage at concentrations of 0 (distilled water), 70, 140 or 280 mg/kg/day to 31 to 36 mated (plug-positive), CD-1 mice/group during gestation days 6 through 15. Body weight (10%) and survival (89%) were reduced; and the incidence of tremors and ataxia increased for high dose dams. Maternal NOEL = 70 mg/kg/day (clinical effects including tremors). Body weight was reduced and the incidence of cleft palate increased for high dose fetuses (8/214 at high dose compared with 0/308 in controls and 1/1580 for laboratory historical controls. Not statistically significant and occurred in the presence of considerable maternal toxicity.) Developmental NOEL = 140 mg/kg/day. UNACCEPTABLE. Upgradeable (individual data not reported.). (Kishiyama and

Gee, 8/18/98).

## GENE MUTATION

13 152753 Pool, B. L. and P. Z. Lin. "Mutagenicity Testing in the *Salmonella typhimurium* Assay of Phenolic Compounds and Phenolic Fractions Obtained from Smokehouse Smoke Condensates". *Food Chemical Toxicology*, 20: 383 - 391 (1982) Smokehouse smoke, used in flavoring meat products, contains phenolic compounds (phenol, cresols, 2,4-dimethyl phenol, brenzacatechine, syringol, eugenol, vanilline and guaiacol). Phenol, (purity $\geq$ 98%) was tested at five concentrations of 0 (DMSO), 0.5, 5, 50, 500 and 5000 µg/plate with and without metabolic activation (Aroclor-induced Sprague-Dawley rats) and evaluated for mutagenicity using five strains of *Salmonella typhimurium*, TA1535, TA1537, TA1538, TA98 and TA100. Quadruplicate plates per concentration. Testing at 5000 ug/plate resulted in a thinning of the background lawn. Phenolic compounds gave negative results. Positive controls were functional. In addition, phenol was tested using several modifications of the assay. These included using S9 from uninduced rats, preincubation before plating, and varying the protein content for activation. Strain TA98 was used for these additional assays. With comparison of induced versus uninduced S9, phenol concentrations (10) up to 9400 ug/plate (100 umol/plate) gave comparable negative results (4 plates per concentration). With preincubation and varying amounts of S9 protein, with TA98, toxicity was noted at 2820 ug/plate (30 umol/plate), showing toxicity at lower concentrations than without preincubation. Phenol was negative under the conditions used. SUPPLEMENTAL study. No worksheet. (Kishiyama and Gee, 8/26/98)

013 152756 Florin, I., L. Rutberg, M. Curvall, and C. R. Enzell. "Screening of Tobacco Smoke Constituents for Mutagenicity using Ames' Test." *Toxicology*, 18: 219 - 232 (1980) Phenol was evaluated with 239 other compounds in tobacco smoke for mutagenicity, using *Salmonella strains* TA98, TA100, TA1535, TA1537 with and without metabolic activation. Phenol was negative. Test concentrations were not given. SUPPLEMENTAL study. No worksheet. (Kishiyama, and Gee, 8/27/98).

**013 152762** Gocke, E., M.-T. King, K. Eckhardt and D. Wild. "Mutagenicity of Cosmetics Ingredients Licensed by the European Communities." *Mutation Research*, 90: 91 - 109 (1981). Phenol was one of 31 chemicals used in cosmetics which were evaluated for mutagenicity in a battery of three assays: *Salmonella*/microsome test, the Basc test on Drosophila and the micronucleus test on mouse bone marrow. Five strains of *Salmonella* were used: TA1535, TA100, TA1538, TA98 and TA1537 with and without activation. In Drosophila, one dose near the $LD_{50}$ was fed to adults and three broods evaluated. For micronuclei, mice (usually 2 male and 2 female) were dosed at 0 and 24 hours and bone-marrow smears prepared at 30 hours. Results: Phenol, tested with *Salmonella* strain TA98 from 0 to an estimated 90 umoles, was positive with activation. Phenol at 50 mM was negative in Drosophila and was also negative for micronuclei induction at doses of 47, 94 and 188 mg/kg i.p., 2 doses at 24 hour interval. **Possible adverse mutagenic** effect with *Salmonella.* SUPPLEMENTAL study. No worksheet. (Kishiyama and Gee, 8/28/98).

**013 152763** Paschin, Yu. V. and L.M. Bahitova "Mutagenicity of benzo[a]pyrene and the Antioxidant Phenol at the HGPRT Locus of V79 Chinese Hamster Cells." *Mutation Research*, 104: 389 - 393 (1982). Phenol was evaluated as a mixture with benzo[a]pyrene (BP) for induction of point mutations in mammalian somatic cells (Chinese hamster V79). Phenol dosages at 250 to 500 µg/ml and BP dosages at 12 to 25 µg/ml increased the frequency of $AG^r$ mutants over the spontaneous level. Phenol up to 250 ug/ml did not affect cell survival.

Mixtures of BP and phenol of 1:10 to 1:40 were tested. There was no effect either blocking or activation of the mixtures as the frequency of $Ag^r$ mutants was the sum of the separate effects. **Possible adverse effect.** SUPPLEMENTAL study. No worksheet. (Kishiyama and Gee, 8/28/98).

Note: Although no one study is complete, there is evidence that phenol caused mutations in *Salmonella* and in mammalian cells in culture. The results in *Salmonella*, however, were not consistent with one study giving negative results (#152753) and one being positive (#152762). With no obvious reason to give more weight to one study over the other, the conclusion is that phenol has a potential for mutagenicity. (Gee, 9/1/98)

## CHROMOSOME EFFECTS

**013 152759** Morimoto, K., S. Wolff and A. Koizumi. "Induction of Sister-Chromatid Exchanges in Human Lymphocytes by Microsomal Activation of Benzene Metabolites." *Mutation Research*, 119: 355 - 360 (1983). Phenol is a metabolite *in vivo* of benzene, a human carcinogen causing, e.g., leukemia. Phenol cannot react with DNA but apparently requires further activation. Whole-blood cultures, stimulated with PHA-M (phytohemagglutinin-M), were exposed to phenol (3 mM) at 40 - 42 hours after initiation of cultures. Cultures continued for a total of 72 hours. Bromodeoxyuridine was present throughout the culture period. The activation system included S9 from rat liver plus an NADPH-generation system. The S9 mix varied from 0% to 90%, expressed as a percentage of undiluted S9 mix. Thirty-five cells were analyzed per concentration of S9 mix. Results: Phenol exposure increased the frequency of SCEs (9.46/cell) compared with controls (7.8) without activation($p < 0.01$). Benzene was inactive without activation. With phenol, peak activity was found with 10% S9 mix (14.03 SCEs/cell) compared with control + 10% S9 mix (7.54/cell). **Possible adverse effect**. SUPPLEMENTAL study. No worksheet. (Kishiyama and Gee, 8/28/98)

## DNA DAMAGE

013 152757 Poirier, M. C., B. T. De Cicco, and M. W. Lieberman. "Nonspecific Inhibition of DNA Repair Synthesis by Tumor Promoters in Human Diploid Fibroblasts Damaged with N-Acetoxy-2-acetylaminofluorene." *Cancer Research,* 35: 1392-1397 (1975). Phenol and 4-nitro-phenol were two of six compounds evaluated *in vitro* using human fibroblasts, WI-38. The purpose was to investigate the potential mechanism of tumor promotion. The effects on DNA repair synthesis and DNA replication were investigated. DNA repair: WI-38 cells were grown to confluency, DNA replication inhibited with hydroxyurea, exposed to the test chemical (10 to 10,000 uM) , damaged with NA-AAF, labeled with $^3$H-thymidine and harvested at 4.25 hr. The DNA was banded on CsCl density gradients. The specific activity of DNA of the gradient fractions was determined by liquid scintillation and absorbance at 260 nm. Phenol at $10^4$ µM inhibited DNA repair synthesis by 50% and DNA replication at $10^3$ uM by 50%. At $10^5$ uM, phenol treatment resulted in nuclear pyknosis and cytoplasmic retraction as evidence of cytotoxicity after 4 hours. The conclusion with phenol (and other compounds) was that there was no specific effect on DNA repair (or other macromolecule synthesis). At inhibitory concentrations, there was evidence of cellular injury. SUPPLEMENTAL study. No worksheet. (Kishiyama and Gee, 8/27/98).

013 152761 Painter, R. B., and R. Howard. "The HeLa DNA-synthesis Inhibition Test as a Rapid Screen for Mutagenic carcinogens. *Mutation Research*, 92: 427 - 437 (1982). A total of 90 chemicals, including phenol, were screened. HeLa cells were grown in the presence of

[$^{14}$C]thymidine for 1 generation time or longer. The compound to be tested was added in fresh, nonradioactive medium for 30 minutes without activation and 1 hour with rat liver S9 activation. After treatment, cells were incubated with [$^{3}$H]thymidine. The ratio of $^{3}$H/$^{14}$C in DNA on filters was determined by scintillation counting and treated expressed as percent of control. The difference should decrease by at least 60% at 30 or 90 minutes after end of exposure to be positive for inhibition of DNA synthesis. For negatives, the initial decrease of 60% was followed by recovery to control values over 30 - 90 minutes. Phenol was evaluated with metabolic activation with an "effective dose" of 2 x $10^{-3}$ M. Effective doses $\underline{\geq}$ 1 mM were considered to be "weaker" DNA-damaging agents. No detailed data for phenol. SUPPLEMENTAL study. No worksheet. (Kishiyama and Gee, 8/28/98).

OTHER:

013 152752. Kada, T., K. Tutikawa and Y. Sadaie. "*In Vitro* and Host-Mediated "rec-Assay" Procedures for Screening Chemical Mutagens; and Phloxine, A Mutagenic Red Dye Detected." *Mutation Research*, 16: 165-174 (1972) A "rec-assay" was used to determine the comparative lethal action on Rec- over Rec+ *Bacillus subtilis* as a tool to indirectly evaluate mutagenicity potential of thirty dyes, including phloxine . Phenol was not included in the chemicals tested. Phloxine increased the inhibition to Rec- over Rec+ cells and mutagenicity confirmed directly in follow-up experiments using *E. Coli* cells. Unclear why this publication was submitted unless to verify the assay. No worksheet. (Kishiyama and Gee, 8/26/98).

013 152755 Chung, King-Thom, G.E. Fulk, and A.W. Andrews. "Mutagenicity Testing of Some Commonly Used Dyes." *Applied and Environmental Microbiology*, 42: 641 - 648 (1981) Phenol red dye [phenolsulfonphthalein] was included with a series of 17 dyes for evaluation of potential mutagenicity. The compounds were tested with *Salmonella typhimurium* strains TA1535, TA1537, TA1538, TA98 and TA100, with and without rat liver metabolic activation with a 30 minute preincubation period before plating. There were duplicate plates with a repeat trial. Phenol red (5 - 5000 µg/plate, 10 concentrations with TA98) with and without metabolic activation was mutagenic at the 1000 ug/plate and above. SUPPLEMENTAL study (test material not phenol) No worksheet (Kishiyama and Gee, 8/27/98)

013 152760 Malcolm, A. R., L. J. Mills and E. J. McKenna. " Effects of Phorbol Myristate Acetate, Phorbol Dibutyrate, Ethanol, Dimethylsulfoxide, Phenol, and Seven Metabolites of Phenol on Metabolic Cooperation between Chinese Hamster V79 Lung Fibroblasts." *Cell Biology and Toxicology*, 1: 269 - 283 (1985). Chinese hamster V79 cells (HGPRT+, HGPRT-) were used. Cytotoxicity was determined by colony formation following a 48-hour exposure to the chemicals in the presence of 6-thioguanine. For the assay of metabolic cooperation, mutant and wild-type V79 were co-cultivated. Each culture dish contained 100 mutant cells and 400,000 wild-type cells. The test material and 6-TG were added for 48 hours. Incubation continued for 4-5 days and macroscopic colonies were counted. Compounds reducing metabolic cooperation reduce the transfer of 6-TG and result in an increase in colonies while those increasing cooperation (transfer of molecules) reduce the number of viable mutant colonies. Phenol had no effect on metabolic cooperation but four phenol metabolites at 1-3 µg/ml (1,4-benzoquinone, catechol, hydroxyquinol and quinol) inhibited metabolic cooperation and another (2-methoxyphenol [methylated deriviative of catechol]) enhanced metabolic cooperation. Data were presented in graphic form. SUPPLEMENTAL study. No worksheet. (Kishiyama and Gee, 8/28/98)

013 152764 Nagel, R., H. I. Adler and T .K. Rao. "Induction of Filamentation by Mutagens and Carcinogens in a lon $^{-}$ Mutant of *Escherichia Coli*." *Mutation Research*, 105: 309 - 312

(1982). Phenol was included in a group of thirteen chemicals to study their effects on filamentation as a possible means to evaluate mutagenicity potential. The chemicals were tested with *E. Coli* $lon^-$ mutants with exposure of 3 - 4 hours with activation, if necessary (not stated for phenol). Cells were deposited on slides, covered with a cover slip, and incubated for an additional 3 hours. Cells in at least 10 microscopic fields were scored for filaments - cells at least 10 times the normal length. Phenol did not induce filamentation when tested at 10, 100 or 500 ug/ml. SUPPLEMENTAL study. No worksheet. (Kishiyama and Gee, 8/28/98).